

Characterizing the Variability of LD50 Values in Acute Toxicity Studies: Implications for Alternative Methods Development

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In vivo LD50 values are often used as reference data to evaluate alternative methods to estimate acute toxicity. However, to achieve a fair assessment of alternative methods, it is important to determine the extent to which in vivo studies vary or predict themselves. We obtained LD50 values from multiple databases, including the NLM's Hazardous Substances Data Bank and ChemIDplus, the OECD's eChemPortal, and the JRC's AcutoxBase, yielding a total of 27,380 oral LD50 values representing 11,276 unique chemicals and 13 species. All chemicals with ≥ 5 studies had variable LD50s spanning at least one order of magnitude, with some ranging over four orders of magnitude, not only across rat studies but also across multiple species. These results underscore the importance of considering an appropriate margin of uncertainty when using in vivo acute oral toxicity data for the assessment of alternative methods. U.S. Federal funds from NIEHS/NIH/HHS contract HHSN273201500010C supported this study.